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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/017,621	12/07/2001	Susan M. Freier	RTS-0350	6422

7590 07/01/2004

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EXAMINER	
SCHULTZ, JAMES	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 07/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/017,621	FREIER ET AL.	
	Examiner	Art Unit	
	J. Douglas Schultz, Ph.D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-20* is/are pending in the application.

4a) Of the above claim(s) *15-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 4-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12-7-2001*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments, Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on April 21, 2004 is acknowledged. The traversal is on the ground(s) that all three of the Groups in this restriction contain claims with the same technical features, namely, a compound targeted to a nucleic acid encoding PCTAIRE protein kinase 1 (SEQ ID NO:3).

The fact that the Groups share a technical feature is not the proper criteria for determining whether Groups are restrictable, and arguments which rely upon this belief are not considered convincing, because the invention of groups I and III are related to the invention of group II as product and process of use, which can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product antisense oligos can be used as probes for identifying the presence of specific mRNA transcripts in *in situ* hybridization assays, which does not involve administering antisense oligos to cells, tissues, or whole animals as present in group II.

Applicants also argue that there would be no additional search burden on the Examiner if the restriction is not made, and assert that any search performed to identify art relating to a compound targeted to a nucleic acid molecule encoding PCTAIRE protein kinase 1 (SEQ ID NO:3) which inhibits expression of PCTAIRE protein kinase 1 would also identify relevant art to any methods of inhibiting the expression of protein kinase 1 using compounds targeted to a

nucleic acid molecule encoding PCTAIRE protein kinase 1 (SEQ ID NO:3). This is not adopted, because searching the art for compounds is considered to constitute a different search than that done for methods of use, particularly including treatment, because methods of treatment often require multiple additional steps or contain limitations or requirements that are not inherent in the search for the compounds. The latter is held to be true in the instant case, where hyperproliferative diseases and neurological treatments are claimed. Furthermore, while a search for a compound that inhibits SEQ ID NO: 3 may possibly result in finding art that inhibits specific variants while not inhibiting others, such a search is not considered to be co-extensive, because PCTAIRE 1B is a different transcript than that for SEQ ID NO: 3 as recited in claim 1. As discussed in the restriction requirement, it is considered a burden on the Office to search and examine more than one sequence in an application.

Applicants also argue that the claims identified in Groups II and III are dependent claims upon claim 1, and are thus related. This is considered to be convincing. Accordingly, claim 1 is hereby treated as a linking claim which links the invention of Groups I-III. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claim 1. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant

application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

The requirement as amended above is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 and 103 that form the basis for the rejections under these sections made in this Office action:

> A person shall be entitled to a patent unless –
>
> 102(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> 103(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 12, and 14 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Okuda *et al.*

The claims of the above invention are drawn to antisense compounds 8 to 50 nucleotides in length that specifically hybridizes with and inhibits the expression of PCTAIRE 1.

The primers used to isolate PCTAIRE 1 as taught by Okuda possess 100% identity with SEQ ID NO: 3 of the instant application, and would thus specifically hybridize with SEQ ID NO: 3. Although this reference does not specifically teach the function of inhibiting applicants' instant SEQ ID NO: 3 as claimed in the present application, the above-listed compounds of the prior art meet all the structural limitations as set forth in the instant claims. Because the sequences are identical to applicant's claimed compounds, in the absence of evidence to the

contrary the compounds of the prior art are thus considered to possess the functional limitations of specifically hybridizing with and inhibiting the expression of applicants' instant SEQ ID NO: 3. Furthermore, the compounds are considered to be in composition with pharmaceutically acceptable diluents, since Okuda discloses their presence in buffers designed for PCR. Support for this conclusion of anticipation and/or obviousness is drawn from MPEP 2112:

> Where applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim **but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection**. "There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102." *In re Best*, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic. Therefore, a 35 U.S.C. 102/103 rejection is appropriate for these types of claims as well as for composition claims. *Emphasis supplied.*

In rejecting the claims of the above under 35 U.S.C. 102 and 103, a prima facie case has been established by the examiner whereby the burden of proof in showing that the claimed compounds are not anticipated by the compound of the prior art as stated lies with the applicant, as per MPEP 2112.01:

> Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433.

Thus, in the absence of evidence to the contrary, the antisense compounds of claims 1, 2, 12, and 14 of the instant application are considered anticipated and/or obvious as outlined above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, and 4-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Okuda *et al.* (Oncogene (1992) 7:2249-58), in view of Charrasse *et al.* (Cell Growth and Diff. (1999) 10:611-620), Taylor *et al.* (Drug Disc. Today, (1999). 4(12)562-567), and Baracchini *et al.* (uspn 5,801,154).

The invention of the above claims is drawn to antisense compounds that target PCTAIRE 1, or said compounds comprising internucleoside, nucleobase, and 2' modifications, chimeras, or compositions comprising said compounds and pharmaceutically acceptable diluents thereof.

Okuda *et al.* teach the cDNA sequence encoding PCTAIRE 1. Okuda et al. does not teach antisense sequences comprising internucleoside, nucleobase, and 2' modifications, chimeras, or

compositions comprising said compounds and pharmaceutically acceptable diluents or delivery systems thereof.

Charrasse *et al.* teach that PCTAIRE1 is a member of the cyclin dependent kinase subfamily, which are highly expressed in post-mitotic tissue. Charrasse *et al.* suggest that this protein may be involved in not only the regulation of cellular proliferation, but also may control the state of differentiation. Charrase also teaches a PCTAIRE-null mutant protein that eliminates PCTAIRE 1 activity, indicating the desirability of studying this protein via mechanisms of inhibition.

Taylor et al. teach the inhibition of expression of any protein using a known cDNA sequence to generate antisense oligos that target that and inhibit the expression of that protein, and also teach that with software analysis and high affinity oligos, one needs to screen only 3-6 oligos to find one that inhibits its target 66-95% (p. 565).

Baracchini et al. teaches modifications of antisense compounds comprising sugar, nucleobase, 2' modifications, chimeras, and compositions comprising said compounds and pharmaceutically acceptable diluents thereof. Baracchini et al. also teach targeting specific regions of a gene including the 5'-untranslated, start codon, coding, stop codon, or 3'-untranslated regions, and demonstrate the methods necessary to achieve gene inhibition.

It would have been obvious to one of ordinary skill in the art to use the cDNA sequence of Okuda to generate antisense sequences as taught by Taylor *et al.* and Baracchini *et al.* for inhibition of PCTAIRE 1 expression, and further, it would have been obvious to one of ordinary skill in the art to incorporate modifications as taught by Baracchini et al. into said antisense compounds. One would have been motivated to create such compounds because Charrasse teach

that PCTAIRE1 is a member of the cyclin dependent kinase subfamily, and is highly expressed in post-mitotic tissue. Furthermore, Charrasse *et al.* suggest that this protein may be involved in not only the regulation of cellular proliferation, but also may control the state of differentiation. Charrase finally teaches a PCTAIRE-null mutant protein that eliminates PCTAIRE 1 activity, indicating the desirability of studying this protein via mechanisms of inhibition. One would have been motivated to modify said antisense compounds as taught by Baracchini et al., because both Taylor *et al.* and Baracchini et al. teach that such modifications increase an antisense compound's cellular uptake, target affinity and resistance to degradation. Finally, one would have a reasonable expectation of success given that Okuda teaches the cDNA sequence, and because Taylor teaches that with software analysis and high affinity oligos, one needs to screen only 3-6 oligos to find one that inhibits its target 66-95%, and finally since Baracchini et al. teach all the steps and reagents required for making modified antisense compounds targeted to distinct regions of a target gene, the steps of which are routine to one of ordinary skill in the art.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Douglas Schultz, Ph.D. whose telephone number is 571-272-0763. The examiner can normally be reached on 8:00-4:30 M-F.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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